

## Claims

✓  
1. The method of synthesizing phenstatin comprising the steps of:  
oxidizing 3-(tert-butyl dimethylsilyl)oxy-4-methoxybenzaldehyde with  
potassium permanganate to form the corresponding carboxylic acid;

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*Sub. B1*  
converting said carboxylic acid to the corresponding acid chloride;

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treating said acid chloride with the lithium derivative obtained from 3,  
4, 5-trimethoxybenzene and t-butyllithium to form a protected product;

and deprotecting said protected product to form phenstatin.

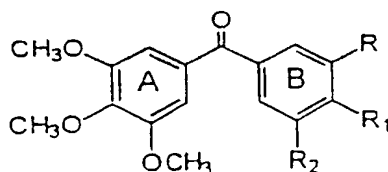
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2. The method of synthesizing phenstatin prodrug comprising the steps of:  
phosphorylating phenstatin with dibenzylphosphite in the presence of  
bromodichloromethane to form a phosphate ester;

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cleaving the benzyl groups from said phosphate ester by means of  
catalytic hydrogenolysis; and

reacting the cleaved phosphate ester with sodium methoxide to produce  
the phenstatin sodium phosphate prodrug.

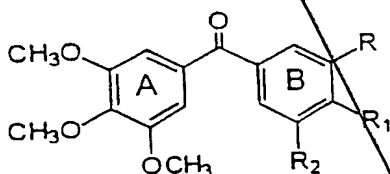
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3. The method of inhibiting cancer cell growth and tubulin polymerization  
in an environment inflicted therewith comprising: introducing into said  
environment a pharmaceutically acceptable carrier and a small but effective  
amount of phenstatin prodrug.

4. Phenstatin prodrugs and derivatives thereof having the structure:



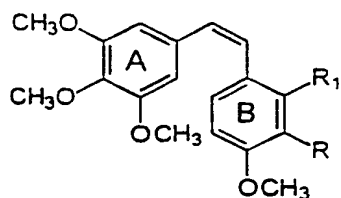
wherein when  $R=H$  and  $R_1 = OCH_3$ ,  $R_2$  is  $OPO_3NA_2$ ,  $OCOCH_3$ ,  $H$ , or  $OCH_3$  and when  $R=R_2$ ,  $R_2$  is  $OCH_3$ ,  $CH_3$ ,  $CL$  or  $F$  and  $R_1$  is  $H$  and when  $R_1=R_2$ ,  $R_2$  is  $OCH_3$  or  $OCH_2O$  and  $R$  is  $H$ .

5. The method of inhibiting human cancer cell growth in a host inflicted therewith comprising administering to said host in pharmaceutically acceptable carrier a small but effective amount of a compound selected from the group consisting of phenstatin, phenstatin prodrug and the derivatives thereof having the structure.



wherein when  $R=H$  and  $R_1 = OCH_3$ ,  $R_2$  is  $OPO_3NA_2$ ,  $OCOCH_3$ ,  $H$ , or  $OCH_3$  and when  $R=R_2$ ,  $R_2$  is  $OCH_3$ ,  $CH_3$ ,  $CL$  or  $F$  and  $R_1$  is  $H$  and when  $R_1=R_2$ ,  $R_2$  is  $OCH_3$  or  $OCH_2O$  and  $R$  is  $H$ .

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2, Combretastatin A-2

1a, R = OH, R<sub>1</sub> = OH

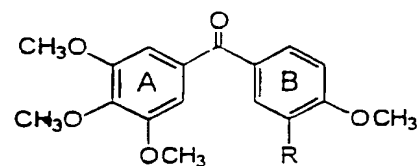
Combretastatin A-1

1b, R = OH, R<sub>1</sub> = H

Combretastatin A-2

1c, R = OSi(CH<sub>3</sub>)<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub>, R<sub>1</sub> = H1d, R = OPO<sub>3</sub>Na<sub>2</sub>, R<sub>1</sub> = H

Combretastatin A-4 prodrug

1e, R = R<sub>1</sub> = H3a, R = OSi(CH<sub>3</sub>)<sub>2</sub>C(CH<sub>3</sub>)<sub>3</sub>

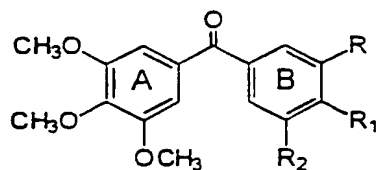
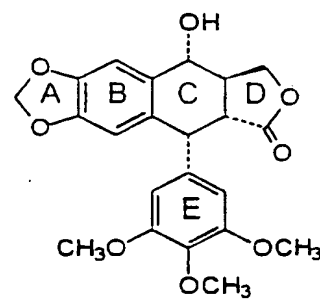
3b, R = OH, Phenstatin

3c, R = OPO<sub>3</sub>(C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>)<sub>2</sub>3d, R = OPO<sub>3</sub>Na<sub>2</sub>

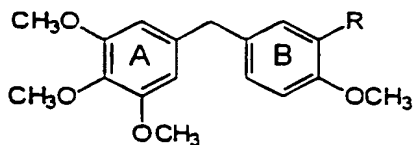
Phenstatin prodrug

3e, R = OCOCH<sub>3</sub>

3f, R = H

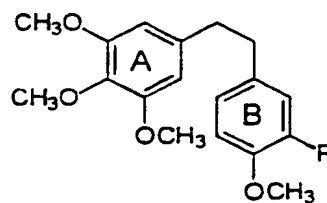
4a, R = H, R<sub>1</sub>, R<sub>2</sub> = OCH<sub>2</sub>O4b, R = R<sub>2</sub> = CH<sub>3</sub>, R<sub>1</sub> = H4c, R = H, R<sub>1</sub> = R<sub>2</sub> = OCH<sub>3</sub>4d, R = R<sub>2</sub> = OCH<sub>3</sub>, R<sub>1</sub> = H4e, R = R<sub>2</sub> = Cl, R<sub>1</sub> = H4f, R = R<sub>2</sub> = F, R<sub>1</sub> = H

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7a, R = OH

7b, R = H



8a, R = OH

8b, R = H

Figure 1.

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